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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,024	08/28/2001	Lance E. Steward	17452 (BOT)	7269

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EXAMINER

SHAHNAN SHAH, KHATOL S

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/942,024

Applicant(s)

STEWART ET AL.

Examiner

Khatol S Shahnan-Shah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 35-53 is/are pending in the application.
- 4a) Of the above claim(s) 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 35, 36 and 38-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 35-53 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5</u> . | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

1. Applicants' preliminary amendment A, received 7/28/2003, paper # 10 is acknowledged.

Claims 1-34 were canceled without prejudice.

Election/Restrictions

2. Applicants' election without traverse of July 25, 2003, paper # 10 is acknowledged.

Applicants elected group II, claims 35-53, which are drawn to a method of determining protease activity of a toxin. Applicants have elected species BoNT/A substrate as set forth in claim 36.

3. Claims 35-53 are pending. Claim 37 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected invention.

Information Disclosure Statement

4. Applicants' Information Disclosure Statement, received 12/26/2001, paper # 5 is acknowledged. The references have been considered by the examiner.

Drawings

5. The drawings are objected to by the Draftsperson under 37 CFR 1.84 or 1.152. See attached form PTO 948.

Specification

6. The disclosure is objected to because of the following informalities:

The use of the abbreviations i.e. SNAP, VAMP, and FLAG have been noted in this application. Full name and description of these abbreviations are required when they appear first time in the specification.

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The use of the trademarks have been noted in this application (i.e. specification pages 4-11, 14, 20 etc). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Appropriate corrections are required.

Claim Objections

7. Claims 39 and 40 are objected to under 37 CFR 1.75(c) as being in improper form because the claims are multiple dependent claims. See MPEP § 608.01(n).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 35, 36, 38, 39, 41, 42, 44, 45, 47, 48 and 53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 61, 62, 63, 67, 71, 72, 73, 74, 76, 77, 78, 79, 80, 81, and 82 of copending Application No. 10261161. Although the conflicting claims are not identical, they are not patentably distinct

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from each other because the claims of both applications are drawn to a method of determining clostridium toxin activity.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 49-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for at most 5% cleavage of clostridial toxin substrate, does not reasonably provide enablement for at least 90%, at most 25%, at most 15% cleavage. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The instant specification invites the skilled artisan to experiment. The factors, which must be considered in determining undue experimentation are set forth in In re Wands USPQ2d

14000. The factors include

- 1) quantity of experimentation necessary,
- 2) the amount of guidance presented,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the predictability of the art and the
- 7) breadth of the claims.

Claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for at most 5% cleavage of clostridial toxin substrate (example 1) is not

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enabled for at least 90%, at most 25%, at most 15% cleavage and does not reasonably provide enablement for any other embodiments encompassed by the claims. The specification prophetically mention other cleavage rates in pages 35 and 36 but the sole example in page 116 only shows a 5% cleavage. The instant specification invites the skilled artisan to experiment. it is noted that the working example is limited to 5% cleavage. Such is not seen as sufficient to support the breadth of the claims; wherein the scope of the claims encompasses broad ranges of substrate cleavage.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 35-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what applicants intend in recitation of “under conditions suitable” in claim

35. What constitute the metes and bounds of “suitable” conditions?

It is not clear what applicants intend in recitation of “under the appropriate conditions” in claim 35. What constitute the metes and bounds of “appropriate” conditions?

It is not clear what applicants intend in recitation of “a BoNT/A recognition sequence” in claim 36.

Claim 42 contains the trademark/trade name BOTOX. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or

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trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a sample or a crude cell lysate isolated from a toxin and, accordingly, the identification/description is indefinite.

Claims 39 and 40 are reciting, “ wherein said sample is isolated clostridial toxin”. It would be proper and clear if the claims recite, “ wherein said sample is ~~an~~ isolated clostridial toxin”.

It is not clear what applicants intend in recitation of “ wherein the conditions suitable for clostridial toxin protease activity are selected such that assay is linear” in claim 53. How one can select such conditions?

The terms "at most" and “ at least” in claims 49-52 are a relative terms which renders the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

It is not clear what applicants intend in recitation of “ at one or more later time intervals” in claim 48. It is not clear what constitutes the metes and bounds of time intervals.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 35-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al. (US 5,965,699) in view of Clegg (Current Opinion in Biotechnology Vol. 6, pp 103-110, 1995).

Claims are drawn to a method of determining protease activity using fluorescence resonance energy transfer.

Schmidt et al. teach a method of determining protease activity using a labeled based assay (see abstract and claims). Schmidt et al. teach a botulinum toxin substrate and BoNT A peptide sequence (see claim 1). Schmidt et al. also teach BOTOX (see column 12, lines 15-20). Schmidt et al. teach detecting increase or decrease protease activity (see claim 9) and comparing the activity to a control. Schmidt et al. teach using fluorescamine as a fluorophore. Schmidt et al. do not teach FRET. However, Clegg teaches utility of fluorescence resonance energy transfer in biological assays and for study of enzymes (see abstract and page 106 under biotechnological applications).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the method taught by Schmidt et al. with well known FRET method taught by Clegg to obtain the claimed method.

One having ordinary skill in the art would have been motivated by the teachings of Clegg that FRET assays can be exploited for fluorometric enzyme assays. (see page 106 under biotechnological applications) to use FRET assay for determining protease activity of botulinum toxins.

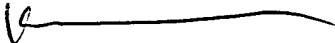
Conclusion

16. No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on Monday through Friday from 7:30 AM - 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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September 21, 2003


RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER